RESPONSE

A. Status of the Claims

Claims 38-60 were pending at the time of the Action. Claims 47, 48, and 55-60 have been withdrawn. Claims 39-46 and 48 have been cancelled. Claims 38, 47, 49, 53, and 54 have been amended. No new matter was added by these amendments.

B. Claim Objections

Claims 38-46 and 49-54 were objected to for reciting the indefinite article "an amino acid sequence" and for reciting a plurality of unelected inventions. Claim 38 currently recites "[a]n isolated hyperimmune serum-reactive antigen fragment comprising an amino acid sequence encoded by a nucleic acid molecule fragment of SEQ ID NO:110 and comprising amino acids 4-37, 40-46, 52-57, 199-205, 222-229, 236-244, 250-267, 269-282, 27-197, 86-109, and/or 104-127 of SEQ ID NO:288." The remaining objected claims ultimately depend from Claim 38. This objection is moot in view of the language of current claim 38.

Claim 39 was objected to for reciting claim limitations directed to Tables 1 and 3. Claim 39 has been cancelled. This objection is moot.

C. Specification Objections

The abstract was objected to for not being on a separate page in the specification. Applicants note that this requirement does not apply to § 371 national stage applications such as this. *See* MPEP §608.01(b). Applicants respectfully request that this objection be withdrawn.

D. Rejections Under 35 U.S.C. § 101

Claims 38-44 are rejected under 35 U.S.C. § 101 for being directed to a product of nature. Claim 38 is currently directed to "[a]n isolated hyperimmune serum-reactive antigen fragment," and claims 39-44 ultimately depend from claim 38. The rejection is moot.

E. Rejections Under 35 U.S.C. § 112

Claims 38-46 and 49-54 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. In particular, it is asserted that the specification is not enabling for vaccines that will treat or prevent *H. pylori* infection.

The present specification satisfies the enablement requirement because it teaches one of skill in the art how to make and use the claimed invention without undue experimentation. The specification provides the structure of and particular immunogenic fragments of SEQ ID NO:288, which was identified using sera from individuals with antibodies against *H. pylori* (*see e.g.,* Specification, Example 3, and Table 1). In other words, this sequence was identified because of a demonstrated ability to stimulate an immune response in a subject. Moreover, on page 67 the specification discloses specific immunogenic epitopes within SEQ ID NO:288. The specification further teaches that hyperimmune serum reactive antigens or antigenic fragments thereof can be made by recombinant protein expression, in vitro translation, or peptide synthesis (Specification, page 15, first paragraph). The antigenicity of a particular sequence can be confirmed by seeing if it is bound by antibodies in sera from individuals with antibodies against *H. pylori* as described in Example 5 of the specification. The specification also discloses a pharmaceutical composition that is "a vaccine for preventing or treating an infection caused by *H. pylori* and/or other pathogens against which the antigens have been included in the vaccine." (Specification, page 38, fourth paragraph).

Accordingly, the specification teaches a person of ordinary skill in the art how to make and use the currently claimed pharmaceutical composition, including a vaccine.

F. Rejections Under 35 U.S.C. § 102

1. The Claims Are Novel Over Ludevid

Claims 38-39 and 41-43 under 35 U.S.C. § 102(e) are rejected as being anticipated by Ludevid *et al.* (U.S. Patent 7,297847). Specifically, it is asserted that Ludevid disclose amino acid sequences that are 100% identical to amino acids 98-113 and 97-114 of SEQ ID NO: 288.

Current claim 38 currently recites "[a] pharmaceutical composition comprising an isolated hyperimmune serum-reactive antigen fragment comprising an amino acid sequence encoded by a nucleic acid molecule fragment of SEQ ID NO:110 and comprising amino acids 4-37, 40-46, 52-57, 199-205, 222-229, 236-244, 250-267, 269-282, 27-197, 86-109, and/or 104-127 of SEQ ID NO:288." The claims are not anticipated because Ludevid does not disclose a fragment that comprises amino acids 4-37, 40-46, 52-57, 199-205, 222-229, 236-244, 250-267, 269-282, 27-197, 86-109, and/or 104-127 of SEQ ID NO:288. Applicants, therefore, request the withdrawal of this rejection.

2. The Claims Are Novel Over Tomb

Claims 38-44 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tomb. The Action asserts that Tomb teaches a hyperimmune serum-reactive antigen comprising SEQ ID NO:288. Applicants traverse.

A claim cannot be anticipated by a reference if the allegedly anticipatory disclosure is not enabled. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. MPEP § 2121.01; *see also Elan Pharms, Inc. v. Mayo Found. for Med. Educ. & Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002) (stating "The anticipating reference 'must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.'"). In *Impax Labs v. Aventis Pharmaceuticals*, Impax asserted that Aventis' '814 Patent, related to the use of riluzole to treat amyotrophic lateral

sclerosis (ALS), was invalid and unenforceable on the basis of a prior art reference, the '940 Patent. The district court found the '904 Patent was not an enabling prior art reference and therefore was not anticipating prior art. Specifically, the court found that "(1) formula I encompasses a particularly large number of compounds; (2) riluzole was not meaningfully discussed in the treatment of medical conditions associated with the effects of glutamate; (3) the language of the '940 patent itself created 'substantial uncertainty' regarding use of glutamate inhibiting compounds in the treatment of ALS; and (4) the language in the '940 patent discussing conditions implicating glutamate is speculative, at best." *Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.*, No. 2007-1513 (Fed. Cir. 2008). The Federal Circuit affirmed the district court's decision.

Tomb does not anticipate the current claims because Tomb does not provide an enabling disclosure of the claimed composition. Similar to the '904 patent, Tomb describes a particularly large number of sequences, *i.e.*, the results of the whole genome sequencing of *Helicobacter pylori* strain 26695 including about 1.7 million base-pairs, which has been deposited in the NCBI Genbank with the accession AE000511.1. The disclosed full length HP1341 polypeptide (accession NP_208133.1) is one of the hypothetical proteins encoded by this complete genomic sequence and is described as a "siderophore-mediated iron transport protein." Tomb postulates that these sequences may be useful for drug discovery and vaccine development, but there does not appear to be any data demonstrating such an effect or any guidance provided as to which sequences will be effective for these purposes and which will not. No further characterization, in particular no immunology-type of experiments have been done with the sequence. There is no discussion of SEQ ID NO:288 as a component of a pharmaceutical composition. Furthermore, the language in Tomb discussing vaccines and drug discovery is speculative, at best, and does not identify specific sequences for such purposes. *See* Tomb at page 539.

Tomb's guess that one or more of the sequences listed in the article may be useful in a pharmaceutical composition is not enabling as it would require undue experimentation to test all of these sequences in the absence of any guidance as to which sequences would likely be immunogenic and thus useful in a pharmaceutical composition. Accordingly, the current claims are not anticipated by Tomb. Applicants request the withdrawal of this rejection.

3. The Claims Are Novel Over Legrain

Claims 38-46, 49, and 53-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Legrain (WO 02/066501), which is said to disclose fragments of SEQ ID NO: 288. Specifically, it is asserted that Legrain disclose amino acid sequences that are 100% identical to fragments of SEQ ID NO: 288.

As discussed above, a claim cannot be anticipated by a reference if the allegedly anticipatory disclosure is not enabled. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. MPEP § 2121.01; *see also Elan Pharms, Inc. v. Mayo Found. for Med. Educ. & Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002) (stating "The anticipating reference 'must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.'"). Also as discussed above in regard to *Impax Labs,* the district court found that the '904 Patent involved in that case was not an enabling prior art reference and therefore was not anticipating prior art based on the court's findings that "(1) formula I encompasses a particularly large number of compounds; (2) riluzole was not meaningfully discussed in the treatment of medical conditions associated with the effects of glutamate; (3) the language of the '940 patent itself created 'substantial uncertainty' regarding use of glutamate inhibiting compounds in the treatment of ALS; and (4) the language in the '940 patent discussing conditions implicating glutamate is speculative, at

best." *Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.*, No. 2007-1513 (Fed. Cir. 2008). The Federal Circuit affirmed the district court's decision.

Legrain does not anticipate the current claims because Legrain does not provide an enabling disclosure of the claimed composition. Legrain discloses about 1600 protein sequences from the Helicobacter genome identified by a yeast two hybrid system-based experimental setup, therefore having a domain for the putative role in protein-protein interactions ("SID"). Actual data was shown only for 96 of the SIDs (Table 5). Among the numerous SID domains presented, HPO406 with 119 amino acids was shown (SEQ ID NO:3186). Legrain did not appear to consider this particular fragment to be one of the best candidates to show in their protein-protein interaction-related experiments because the HPO406 is not disclosed on Table 5. Legrain does not appear to provide any discussion concerning HPO406 nor does Legrain appear to disclose the use of HPO406 in a vaccine. In addition, Legrain did not show the immunogenicity and/or antigenicity of HPO406 or its subfragments. *See Elan Pharms, Inc.*, 304 F.3d at 1228 (stating "The anticipating reference 'must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.'"). Thus, there is no data demonstrating that HPO406 may be used in a vaccine or any guidance provided as to which of the approximately 1600 sequences will be effective for this purpose and which will not.

Accordingly, the current claims are not anticipated by Legrain. Applicants request the withdrawal of this rejection.

4. The Claims Are Novel Over Kleanthous

The Action also rejects claims 38-46, 49-50, and 53-54 under 35 U.S.C. § 102(b) as being anticipated by Kleanthous (WO 98/43478), which is said to disclose SEQ ID NO: 288 as well as fragments of SEQ ID NO: 288. In addition, Kleanthous is said to disclose that the antigen is immunoreactive with a monospecific hyperimmune antiserum. Applicants respectfully traverse.

As an initial point, the Action's assertion that Kleanthous' SEQ ID NO: 118 shares 100% identity over 154 amino acids of SEQ ID NO: 288 is incorrect (see Action, p. 11). There does not appear to be any significant similarity between the two sequences. Applicants request that the examiner reconsider this assertion.

Kleanthous does not anticipate the current claims because Kleanthous does not provide an enabling disclosure of the claimed pharmaceutical composition. *See* MPEP § 2121.01; *see also Elan Pharms, Inc.*, 304 F.3d at 1228; *Impax Laboratories, Inc.*, No. 2007-1513. Like the Tomb and Legrain references, Kleanthous describes a particularly large number of sequences, *i.e.*, the genomic sequence of a *Helicobacter pylori* strain in companion with about 700 predicted polypeptide sequences. According to the real, wet-lab experiments described in the disclosure, six hypothetical ORFs were selected to be amplified by gene-specific primers. Kleanthous' GHPO 894 was not selected for such further study. Kleanthous postulates that these sequences may be useful in pharmaceutical formulations, but there does not appear to be any data demonstrating this usefulness. In particular, no further characterization steps directed to any of the putative protein compounds were found, and the immunoreactivity of the hypothetical polypeptides have been mentioned just in theory without experimental data (page 60, line 10). Thus, the language in Kleanthous discussing vaccines and drug discovery is speculative, at best. Kleanthous also does not teach the particular fragments of SEQ ID NO:288 recited in claim 38. It would require undue experimentation to test all of these sequences in the absence of any guidance in the Kleanthous specification as to which sequences would likely be immunogenic and thus useful in a pharmaceutical composition.

For at least the reasons above, the current claims are not anticipated by Kleanthous. Applicants request the withdrawal of this rejection.

G. Rejections Under 35 U.S.C. § 103

Claims 50, 51, and 52 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kleanthous in view of Meinke (WO 02/059148). In particular, Meinke is cited as teaching adjuvants that are not disclosed by Kleanthous.

In making a determination as to whether a *prima facie* case of obviousness exists, the examiner should: (A) determine the "scope and content of the prior art;" (B) ascertain the "differences between the prior art and the claims at issue;" (C) determine "the level of ordinary skill in the pertinent art;" and (D) evaluate evidence of secondary considerations. *Graham v. John Deere*, 383 U.S. 1, 17 (1966); *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734; *see also MPEP* § 2141.

With regard to the scope and content of the prior art, the Office has failed to establish that the combination of Kleanthous and Meinke discloses or suggests every element of the rejected claims, namely a pharmaceutical composition comprising the specified fragments of SEQ ID NO:288. Applicants' claimed invention concerns "[a] pharmaceutical composition comprising an isolated hyperimmune serum-reactive antigen fragment comprising an amino acid sequence encoded by a nucleic acid molecule fragment of SEQ ID NO:110 and comprising amino acids 4-37, 40-46, 52-57, 199-205, 222-229, 236-244, 250-267, 269-282, 27-197, 86-109, and/or 104-127 of SEQ ID NO:288." Claim 38. The pharmaceutical composition may further comprise an immunostimulatory substance. Claim 49. The immunostimulatory substance may be "a polycationic polymer, an immunostimulatory deoxynucleotide (ODN), a peptide containing at least two LysLeuLys motifs, a neuroactive compound, alum, or a Freund's complete or incomplete adjuvant." Claim 50.

Kleanthous is relied on as disclosing compositions that comprise *Helicobacter pylori* immunogenic antigens with a immunostimulatory substance. However, Kleanthous does not

anticipate the current claims because Kleanthous does not provide an enabling disclosure of the claimed pharmaceutical composition. *See Impax Laboratories, Inc.*, No. 2007-1513. As discussed above, Kleanthous describes a particularly large number of sequences, *i.e.*, the genomic sequence of a *Helicobacter pylori* strain in companion with about 700 predicted polypeptide sequences. Kleanthous postulates that these sequences may be useful in pharmaceutical formulations, but there does not appear to be any data demonstrating this usefulness and the language discussing pharmaceutical formulations is speculative, at best. Kleanthous also does not teach the particular fragments of SEQ ID NO:288 recited in claim 38.

Meinke does not remedy the failure of Kleanthous to disclose a pharmaceutical composition comprising the specified fragments of SEQ ID NO:288. Meinke is cited only as disclosing immunostimulatory substances including polycationic polymer, an immunostimulatory deoxynucleotide (ODN), a peptide containing at least two LysLeuLys motifs, a neuroactive compound, and alum. Thus, the cited references, alone and in combination, fail to teach or suggest all of the elements of the independent claims, and thus they cannot render the claims obvious.

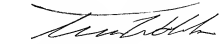
In view of the above, the current claims are non-obvious over the cited references. Applicants, therefore, request the withdrawal of these rejections.

H. Conclusion

Applicants believe this paper to be a full and complete response to the Office Action dated June 10, 2008. Applicants respectfully request favorable consideration of this case in view of the above comments and amendments.

Should the Examiner have any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-5654.

Respectfully submitted,



Travis M. Wohlers
Reg. No. 57,423
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
Telephone: 512/536-5654
Facsimile: 512/536-4598

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